NOVEL LEAD STRUCTURES FOR ANTIMALARIAL FARNESYLTRANSFERASE INHIBITORS

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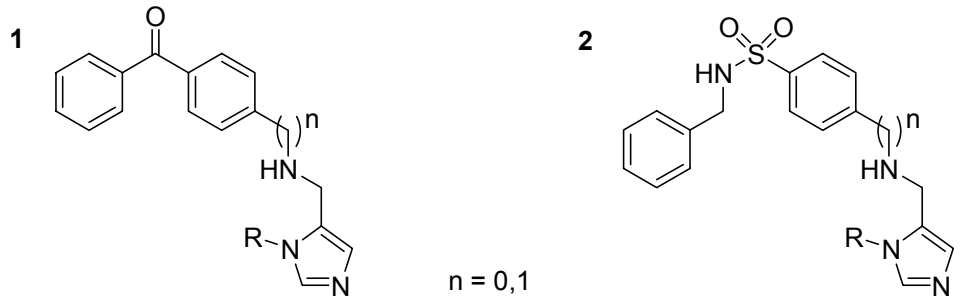
Farnesyltransferases (FTases) were identified in pathogenic protozoa including *Plasmodium falciparum*, the causative agent of malaria tropica [1]. Malaria tropica is the most important protozoa caused disease accounting for 2 to 3 million death cases each year. There is an urgent need for new anti-malarial therapeutics because of the accelerated occurrence of malaria parasites resistant to chloroquine and other commonly used drugs. For this reason we are searching for novel lead structures for antimalarial farnesyltransferase inhibitors. Previously, we have described the development of p-aminobenzophenone- and sulfonamide-based farnesyltransferase inhibitors with a nitrophenylfurylacryloyl moiety as a substructure which show significant activity (IC_{50}-values in the nanomolar range) as antimalarial agents [2].
FTase is a heterodimeric zinc metalloenzyme. It is already known that benzylimidazole-derivates are excellent cysteine surrogates of CAAX-peptidomimetic farnesyltransferase inhibitors by serving as an alternative ligand for the FTase's active site zinc ion [3].
Therefore, we combined 4-benzophenone- (**1**) and *N*-benzylsulfonamide-based (**2**) analogues with different imidazoles to improve the antimalarial activity.



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